1: Hum Gene Ther. 1997 Apr 10;8(6):719-27.

HER2-targeted gene transfer.

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Selective transfer of genes to specific cells remains a barrier to successful utilization of somatic gene therapy. We hypothesized that the human epidermal growth factor receptor-2 (HER2, also called ErbB2), a membrane tyrosine kinase highly expressed in many epithelial tumors, could be an immunological target for gene transfer. To test this hypothesis in vitro, we non-covalently linked a luciferase expression vector (pRSVLuc) to a humanized HER2 antibody (rhuMAbHER2) covalently modified with poly-L-lysine bridges (PL). This complex (PL-rhuMAbHER2) was tested for its ability to direct gene transfer to HER2 expressing cells in vitro using NIH3T3 (HER2 nonexpressing) and NIH3T3.HER2 (HER2 expressing) cell lines as a model system. Twenty-four hours after exposing NIH3T3.HER2 cells to the PL-rhuMAbHER2-pRSVLuc complexes and 100 microM chloroquine, luciferase expression was 180-fold higher than that obtained from a conjugate made with an isotype-matched antibody against an irrelevant target. Exposing the HER2-expressing adenocarcinoma cell lines BT474 and SKBR3 to the HER2-targeted complexes also resulted in successful gene transfer and expression. Gene transfer was specific for the HER2 receptor, because preincubation of HER2-expressing cells with unconjugated rhuMAbHER2 decreased complex-mediated luciferase expression by 95%. These studies suggest that HER2 may be an appropriate target for selective gene transfer and that PL-rhuMAbHER2-DNA complexes may be a useful vehicle for directing gene transfer to cells that express HER2.

PMID: 9113511 [PubMed - indexed for MEDLINE]